

WEST

L5: Entry 7 of 50

File: USPT

Nov 21, 2000

DOCUMENT-IDENTIFIER: US 6150102 A

TITLE: Method of generating nucleic acid oligomers of known composition

DEPR:

A custom set of soluble oligomers of known composition is obtained by locally denaturing double-stranded complexes of selected depots of the intact array comprising the desired oligomers, and collecting the oligomers released from the selected depots ((5) in FIG. 2) into the buffer solution in which the array is immersed ((8) in FIG. 2). Denaturation of oligomer complexes at selected depots can be achieved by any of the nucleic acid-denaturing treatments known to those skilled in the art of nucleic acid biochemistry. Those skilled in the art appreciate that the melting temperature of a double-stranded oligonucleotide complex is dependent on the length, nucleotide sequence, and chemical structure of the complex, and on the ionic strength and chemical composition of the solvent (see Sambrook et al., 1989, *supra*, page 11.46).

WEST

L5: Entry 17 of 50

File: USPT

Dec 28, 1999

DOCUMENT-IDENTIFIER: US 6007987 A

TITLE: Positional sequencing by hybridization

BSPR:

The array is also useful for the purification of nucleic acid from a complex mixture for later identification and/or sequencing. A purification array comprises sufficient numbers of probes to hybridize and thereby effectively capture the target sequences from a complex sample. The hybridized array is washed to remove non-target nucleic acids and any other materials which may be present and the target sequences eluted by denaturing. From the elution, purified or semi-purified target sequences are obtained and collected. This collection of target sequences can then be subjected to normal sequencing methods or sequenced by the methods described herein.

Display Format:

DERWENT-ACC-NO: 2001-082770
 DERWENT-WEEK: 200121
 COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Substrate carrying immobilized nucleic acid molecule, useful as DNA array, comprises a carrier comprising a base material and a compound having carbodiimide or isocyanate group, and nucleic acids

INVENTOR: ICHIHARA, T; MATSUMURA, Y ; SHIOHATA, N ; SUZUKI, O

PRIORITY-DATA: 1999JP-0173966 (June 21, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2001066304 A	March 16, 2001	N/A	016	G01N033/53
EP 1063301 A2	December 27, 2000	E	021	C12Q001/68

INT-CL (IPC): C12M 1/00; C12M 1/40; C12N 15/09; C12Q 1/68; G01N 31/22; G01N 33/53; G01N 33/566

ABSTRACTED-PUB-NO: EP 1063301A

BASIC-ABSTRACT:

NOVELTY - A nucleic acid immobilized substrate (I) comprising a carrier which comprises a base material and a compound having a carbodiimide or an isocyanate group carried by the base material, and same or different kinds of nucleic acids immobilized in the form of dots through the carbodiimide group or isocyanate group at a number of sites on the carrier is new.

USE - (I) is useful as a DNA array and as a DNA chip.

ADVANTAGE - DNAs are stably immobilized on the substrate without any limitations concerning the number of chains or length of the nucleic acids, and thus various kinds of nucleic acids can simultaneously be handled on the same base material. Since nucleic acids are securely bound to the carrier through covalent bonds, nucleic acid immobilized substrates are useful as DNA chip of excellent reproducibility and quantification characteristics.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KMC](#) | [Drawn Desc](#) | [Image](#)

37. Document ID: WO 9515970 A1

L2: Entry 37 of 37

File: DWPI

Jun 15, 1995

DERWENT-ACC-NO: 1995-224282
 DERWENT-WEEK: 200006
 COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Immobilising synthetic nucleic acid on solid support - by incubation in presence of salt or cationic detergent, for use in hybridisation assays, sequencing and analysis of polymorphism

INVENTOR: KNAPP, M R; NIKIFOROV, T

PRIORITY-DATA: 1994US-0341148 (November 16, 1994), 1993US-0162397 (December 6, 1993)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9515970 A1	June 15, 1995	E	061	C07H019/00

INT-CL (IPC): C07H 19/00; C07H 21/00; C12N 11/08; C12Q 1/68

ABSTRACTED-PUB-NO: US 5610287A

BASIC-ABSTRACT:

Synthetic nucleic acid (I) is immobilised on a solid support by incubation in presence of salt or cationic detergent, then washing the support with aq. soln..

USE - Immobilised (I) are used (a) to capture specific nucleic acid analyte (A) by hybridisation, for subsequent detection of (A), partic. where (A) has been amplified by PCR; or (b) where (I) is a primer for template-dependent extension of (I) in presence of nucleic acid from a target organism, a polymerase and at least 1 dideoxynucleotide complementary to the single nucleotide of a single nucleotide polymorphism. The dideoxynucleotide incorporated at the 3' end is then identified. These methods are useful in hybridisation assays, sequencing and analysis of genomic polymorphism.

ADVANTAGE - (I) are rapidly and inexpensively immobilised by a very simple procedure. No modification of (I) or support is required and both DNA (opt. double stranded) and RNA can be immobilised. At least 500 pmole (I) can be fixed in a microtitre plate well and will remain fixed after incubation with 0.5M NaOH at high temp. or washing with buffers contg. NaCl and nonionic surfactant.

ABSTRACTED-PUB-NO:

WO 9515970A EQUIVALENT-ABSTRACTS:

A method for non-covalently immobilizing a synthetic nucleic acid molecule on a solid support which is a hydrophilic polystyrene solid support containing a hydrophilic group selected from the group consisting of -OH, -C=O, and -COOH, or a glass solid support, said method comprising the steps:

(a) contacting said support with a solution having a pH of from about 6 to about 8, and containing said nucleic acid and (1) a cationic detergent selected from the group consisting of 1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride provided at a concentration of from about 30 mM to about 100 mM, and octyldimethylamine hydrochloride provided at a concentration of from about 50 mM to about 150 mM or (2) NaCl provided at a concentration of from about 50 mM to about 250 mM, to thereby non-covalently immobilize said nucleic acid to said support, wherein:

(i) when said cationic detergent is 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide-1,3-hydrochloride, said support is selected from the group consisting of glass or said hydrophilic polystyrene;

(ii) when said cationic detergent is octyldimethylamine hydrochloride, said support is said hydrophilic polystyrene; and

(iii) when said solution contains said NaCl, said support is said hydrophilic polystyrene; and

(b) subsequently washing said solid support with an aqueous solution.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KIMC](#) | [Drawn Desc](#) | [Image](#)

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Terms	Documents
nucleic same immobiliz\$ same carbodiimide	37

[Display](#)

10

Documents, starting with Document: 37

PUB-NO: EP000747703A2

DOCUMENT-IDENTIFIER: EP 747703 A2

TITLE: Method for analyzing biological active substances

PUBN-DATE: December 11, 1996

INVENTOR- INFORMATION:

NAME	COUNTRY
SUZUKI, OSAMU	JP
SASAKI, NAOKAZU	JP
ICHIHARA, TATSUO	JP
OKADA, SANAE	JP

INT-CL (IPC): G01N 33/543; G01N 33/547; G01N 33/58; C12Q 1/68

EUR-CL (EPC): G01N033/543

ABSTRACT:

CHG DATE=19990617 STATUS=0> A method is provided, comprising the steps of reacting a biologically active first substance immobilized on a carrier with a second substance capable of specifically binding the first substance, and detecting a non-bound part of the second substance or a bound part of the second substance indirectly bound to the carrier through binding between the first and second substances so that the first substance or the second substance in a sample is analyzed, wherein the carrier carries a compound having 2 to 100 carbodiimide groups, and the first substance is immobilized on the carrier through the carbodiimide groups so that the active substance such as protein and nucleic acid is bound to the carrier conveniently, efficiently, and tightly.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KWMC](#) | [Drawn Desc](#) | [Image](#)

36. Document ID: JP 2001066304 A, EP 1063301 A2

L2: Entry 36 of 37

File: DWPI

Mar 16, 2001

PUB-NO: JP404325099A
DOCUMENT-IDENTIFIER: JP 04325099 A
TITLE: IMMobilization of NUCLEIC ACID ONTO MEMBRANE

PUBN-DATE: November 13, 1992

INVENTOR-INFORMATION:

NAME

MIYAKOSHI, TERUICHI

IKUTA, YURIKO

COUNTRY

US-CL-CURRENT: 435/6
INT-CL (IPC): C12Q 1/68; C07C 267/00; C12N 15/10

ABSTRACT:

PURPOSE: To accomplish the title immobilization even for short chain nucleic acids, causing no nucleic acid debonding and ensuring hybridization by binding of a nucleic acid to a membrane such as of cellulose through dehydrating condensation using a dehydrating condensation agent having plural functional groups.

CONSTITUTION: In immobilizing a nucleic acid onto a membrane, the nucleic acid is bonded to a membrane of cellulose or polyamide resin through dehydration using a water-soluble dehydrating condensation agent consisting of a compound of the formula (R₁, R₂ and R₃ are each 1-10C alkyl; n in integer of 1-6), its derivative, or a RX (R is H or 1-10C alkyl; X is halogen) adduct thereto [e.g. 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride], thus affording an immobilized nucleic acid fixed onto a membrane to be used for nucleic acid's hybridization. For the dehydrating condensation agent, a compound having such functional groups as SH, OH, amino, COOH and SO₃H groups may also be used.

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Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Draw. Desc	Clip Img	Image
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34. Document ID: US 5610287 A

L2: Entry 34 of 37

File: EPAB

Mar 11, 1997

PUB-NO: JP408023975A

DOCUMENT-IDENTIFIER: JP 08023975 A

TITLE: MATERIAL FOR IMMOBILIZING BIOLOGICALLY ACTIVE SUBSTANCE AND IMMOBILIZING METHOD

PUBN-DATE: January 30, 1996

INVENTOR-INFORMATION:

COUNTRY

NAME

TAKENISHI, SOICHIRO

SUZUKI, OSAMU

IMASHIRO, YASUO

TAKAHASHI, IKUO

SASAKI, NAOICHI

SHIYOUJI, TOMOAKI

MATSUBAYASHI, HIROKO

INT-CL (IPC): C12N 11/08

ABSTRACT:

PURPOSE: To obtain a material composed of a substrate and a polymer compound supported on the substrate and having a carbodiimide group, capable of easily immobilizing a biologically active substance and useful e.g. as immobilized enzyme, antibody or antigen or a diagnostic having immobilized nucleic acid.

CONSTITUTION: This material for immobilizing a biologically active substance is produced by reacting a substrate consisting of a 96-hole microplate made of polystyrene with a diisocyanate compound such as 4,4'-dicyclohexylmethane diisocyanate and a diamine such as 1,4-diaminobutane, adding a solution of a polymer compound having a carbodiimide group and prepared by treating with a carbodiimidation catalyst such as 3-methyl-1-phenylphospholene-1-oxide and incubating the mixture at 60°C for 1hr. An aqueous solution of a biologically active substance such as enzyme, hormone, antigen, antibody, hapten, peptide or DNA is poured into the well and treated at 37°C for 2hr to immobilize the active substance to the material.

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Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Drawn Desc	Image
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33. Document ID: JP 04325099 A

L2: Entry 33 of 37

File: JPAB

Nov 13, 1992

WEST

Generate Collection

Search Results - Record(s) 31 through 37 of 37 returned.

□ 31. Document ID: JP 2000139461 A

L2: Entry 31 of 37

File: JPAB

May 23, 2000

PUB-N0: JP02000139461A

DOCUMENT-IDENTIFIER: JP 2000139461 A

TITLE: SUBTRACTION OF NUCLEIC ACID AND DEVICE THEREFOR

PUBN-DATE: May 23, 2000

INVENTOR-INFORMATION:

NAME

COUNTRY

KIKUCHI, JIRO

N/A

INT-CL (IPC): C12N 15/09; C12M 1/00; C12Q 1/68

ABSTRACT:

PROBLEM TO BE SOLVED: To provide a method for subtracting nucleic acid, capable of simply recovering a cDNA originated from an mRNA specifically expressed in an objective sample in a high recovery rate, and to provide a device therefor.

SOLUTION: This method for subtracting nucleic acid comprises using a microplate wherein the surfaces of wells are coated with carbodiimide capable of covalently bonding to nucleic acids such as DNA and RNA, bonding and immobilizing the genetic expression products of a control sample to the wells through the carbodiimide, and subsequently adding a complementary single strand cDNA synthesized using an mRNA of the objective sample as a template, thus hybridizing and immobilizing the cDNA with the complementary mRNA immobilized on the wells. By the reaction, the genes removed to recover the cDNA originated from the mRNA specific only to the objective sample.

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Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Draw. Desc.	Image
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□ 32. Document ID: JP 08023975 A

L2: Entry 32 of 37

File: JPAB

Jan 30, 1996

WEST

L2: Entry 22 of 37

File: USPT

Jul 7, 1998

DOCUMENT-IDENTIFIER: US 5776672 A

TITLE: Gene detection method

DEPR:

The examples of the procedure for the immobilization by means of covalent bond are the method in which the surface of the carrier is activated and then the nucleic acid probe is immobilized directly or indirectly through crosslinking agent and the method in which an active functional group is introduced into the nucleic acid probe to be immobilized onto the carrier followed by direct or indirect immobilization. The activation of the carrier surface may be conducted by electrolytic oxidation in the presence of oxidizing agent, or by air oxidation or reagent oxidation, as well as by covering with a film. Useful crosslinking agents may be, but are not limited to, silane couplers such as cyanogen bromide and gamma-aminopropyl triethoxy silane, carbodiimide and thionyl chloride and the like. Useful functional groups to be introduced to the nucleic acid probe may be, but are not limited to, amino group, carboxyl group, hydroxyl group, carbonyl group, phosphate group, aldehyde group and mercapto group. Other highly reactive functional groups may also be employed.

WEST

 Generate Collection

L2: Entry 7 of 37

File: USPT

Oct 31, 2000

DOCUMENT-IDENTIFIER: US 6140135 A
TITLE: Multifunctional surfaces

DEPR:

The immobilization of the molecules is obtained by conventional methods and is dependent of which kind of molecules the array is to include. For example if an array of oligonucleotides is to be produced, the thread or membrane can be preactivated with carbodiimide, (according to Zang Y. et al, *Nucleic Acids Research*, Vol. 19, No. 14, 3929-3933) or with N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) and the oligonucleotide is then covalently coupled through a primary amine or thiol group, respectively, at its end depending on the coupling chemistry. It is also possible to preactivate the thread or membrane with other methods such as with corona discharge treatment or plasma treatment.

WEST

L2: Entry 9 of 37

File: USPT

Sep 5, 2000

DOCUMENT-IDENTIFIER: US 6114117 A

TITLE: Homogeneous diagnostic assay method utilizing simultaneous target and signal amplification

DEPR:

Covalent attachment of the probe to a solid support generally involves modification of the probe at either the 5' or 3' terminus. Terminal modification is preferred in order to lessen interference with target (and target analog) hybridization to the probe. For example, the 5' terminus can be modified by introducing reactive amine moieties (using an automated synthesizer) which can then be used in a coupling reaction with activated supports. Examples of other methods of attachment involve carbodiimide based attachment of nucleic acids to cellulose, sephadex or sephacryl; and immobilization of the nucleic acid via the nucleic acid bases which are coupled to the solid support, and vice versa (Lund, et al., Nucl. Acids Res. 16: 10861-10880(1988).)

DEPR:

The probe is immobilized via carbodiimide (EDC) mediated attachment of the 5' phosphate of the DNA:RNA:DNA chimeric probe to beads which contain reactive surface carboxyls (Bangs Laboratories, Carmel, Ind.) according to the method described by Lund, et al. Nucl. Acids Res. 16: 10861-10880 (1988). Carbodiimide reacts with the 5' phosphate group to form a phosphoramidate, which is then reacted with the carboxyl- containing beads to form a covalent bond between the oligonucleotide and the bead. (Hermanson, Nucleic Acid and Oligonucleotide Modification and Conjugation, Bioconjugate Techniques, Academic Press, pages 649-651) (1995).)

WEST

L2: Entry 8 of 37

File: USPT

Sep 26, 2000

DOCUMENT-IDENTIFIER: US 6124092 A

TITLE: Multiplex polynucleotide capture methods and compositions

DEPR:

In the polynucleotide recovery devices of the invention, the recovery tag binding compounds are attached to the solid support in a manner so as to permit the recovery tag binding compounds to interact with their respective recovery binding tags. A variety of techniques may be used to immobilize the recovery tag binding compounds on the solid support. The specific techniques selected will depend upon the choice of recovery tag binding compounds and solid support materials. Techniques for immobilizing proteins and polynucleotides are well known to persons of ordinary skill in the art of molecular biology. For example, proteins may be conjugated to solid supports through formaldehyde, DMS (dimethyl suberimidate), and reductive amination. Polynucleotides may be conjugated to solid supports through agents such as 1,3-diaminopropane, 3,3'-iminobispropylamine, EDC (1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride), SPDP (N-succinimidyl 3-(2 pyridyldithio propionate)), and SATA (N-succinimidyl S-acetylthioacetate). Examples of moieties for linking oligonucleotides to solid supports can be found in Pon et al, *Biotechniques*, 6:768-775 (1988); Webb, U.S. Pat. No. 4,659,774; Barany et al, PCT patent application PCT/US91/06103; Brown et al, *J. Chem. Soc. Commun.*, 1989:891-893; Dahma et al, *Nucleic Acids Res.* 18:3813-3821 (1990); Beattie et al, *Clinical Chemistry*, 39:719-722 (1993); Maskos and Southern, *Nucleic Acids Res.*, 20: 1679-1684 (1992). The recovery tag binding compounds may be attached to the support through either direct or indirect linkages. The term "direct linkage" refers to the covalent binding of the recovery tag binding compound to the solid support, including covalent bonding through a linker (and optionally a spacer arm). The term "indirect linkage" refers to the

WEST

L3: Entry 7 of 16

File: USPT

Jul 4, 2000

DOCUMENT-IDENTIFIER: US 6083763 A
TITLE: Multiplexed molecular analysis apparatus and method

DEPR:

Nucleic acid probe attachment to glass employs well-known epoxy silane methods (see FIG. 12) described by Southern and others (U. Maskos et al., Nucleic Acids Res (1992) 20:1679-84; S. C. Case-Green et al., Nucleic Acids Res (1994) 22:131-36; and Z. Guo et al., Nucleic Acids Res (1994) 22:5456-65). FIG. 12 is a diagram showing glass and polypropylene surface coupling chemistries. With 3' amine-modified probes, covalent surface densities can be obtained having 10.^{sup.11} molecules/mm.^{sup.2} which is near the theoretical packing density limit. Amino-modified polypropylene is a convenient alternative to a glass substrate since it is inexpensive and optically clear above 300 nm. Amine-modified polypropylene can be converted to a carboxylic acid-modified surface by treatment with concentrated succinic anhydride in acetonitrile. Amine-modified probe is then coupled to this surface by standard carbodiimide chemistry in H_{sub.2}O to yield probes at densities near 10.^{sup.9} /mm.^{sup.2} (see FIG. 12).

WEST

L3: Entry 11 of 16

File: USPT

Nov 16, 1999

DOCUMENT-IDENTIFIER: US 5985548 A

TITLE: Amplification of assay reporters by nucleic acid replication

DEPR:

Reporter conjugates, including the nucleic acid replication substrate and nucleic acid replication conjugate, may contain a molecular spacer segment linking the two functional elements of the conjugate. One purpose of the spacer is to extend the replication segment of the target or binding functions away from the surface of the solid phase support. Useful spacers are well known in the affinity chromatography art. For example, H. Shoot, *Affinity Chromatograph*, (1984), Marcell Deckker, Inc., New York, describes different spacers and their use. Advantageously, the spacer includes a chain of up to about 50 atoms, preferably 5 to 30 atoms. In composition, spacers may be a polyfunctional segment including, but not limited to, one or more of the groups: peptide, hydrocarbon, polyalcohol, polyether, polyamine, polyimine and carbohydrate e.g. -glycyl-glycyl-glycyl- or other oligopeptide, carbonyl dipeptide, and omegaaminoalkane-carbonyl radical such as --NH--(CH₂).sub.2 .sub.2 --CO--, a spermine or spermidine radical, omega-alkanediamine radical such as --NH--(CH₂).sub.2 .sub.6 --NH-- or --HN--CH₂ --CH₂ --NH--. The spacer segment may also be comprised of polymeric units such as polysaccharide, polyethylene oxide radicals, glycetyl, pentaerythritol and like radicals. The spacer segment may be linked directly or linked through a divalent heterobifunctional or homobifunctional couplers, for example SATA (N-succinimidyl S-acetylthioacetate), SMCC (succinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate), p-phenyl diisothiocyanate, dithiobis succinimidyl propionate, 1,4-butanediol diglycidyl ether, a diisocyanate, carbodiimide, glyoxal, glutaraldehyde or sulfosuccinimidyl 6-(4'-azido-2'nitro-phenylamino)-hexanoate.

WEST

L2: Entry 6 of 37

File: USPT

Dec 26, 2000

DOCUMENT-IDENTIFIER: US 6165714 A

TITLE: Devices and methods for detecting nucleic acid analytes in samples

DEPR:

BSA is a particularly useful linker, since it can significantly reduce non-specific binding of nucleic acids to the probes immobilized on a solid surface. BSA also allows efficient replication of the autocatalytic replicable RNA to which it links. The following describes an exemplary protocol for linking RNA probes to a solid support via BSA. Acid washed glass slides are first reacted with glycidyl oxypropyl trimethoxy silane, which generates amine-reactive epoxy groups on the glass. BSA is then coupled to these epoxy groups, and the carboxyl groups on the coupled albumin are activated by, e.g., N-hydroxy-succinamide with a carbodiimide such as 1-cyclohexyl-3(2-morpholino-ethyl)carbodiimide (CMC) or 1-ethyl-3(3-dimethylamino propyl)carbodiimide (EDAC), to generate amine-reactive N-hydroxysuccinamide-esters (NHS). RNA with a 5' terminal amino group is then reacted with the NHS-derivatized albumin.

WEST

 Generate Collection

L2: Entry 10 of 37

File: USPT

Aug 29, 2000

DOCUMENT-IDENTIFIER: US 6110678 A

TITLE: Two-step hybridization and capture of a polynucleotide

DEPR:

The basic protocol included the following steps. A lysate of the sample was prepared by adding a clinical sample (e.g., 500 μ l of sediment from sputum, bronchoalveolar lavage or bronchial washings) to an equal volume of a lysis buffer (2.2 M LiCl, 250 mM HEPES buffer, pH 7.5, containing 4% (w/v) LLS) and organisms in the lysate were heat killed (95.degree. C. for 15 min). If *M. tuberculosis* is present in the clinical sample, a target polynucleotide (e.g., rRNA sequence) derived from *M. tuberculosis* will be present in the lysate. An aliquot (250 μ l) of the lysate was mixed with an equal volume of a solution containing the capture probe specific for the *M. tuberculosis* target sequence and an immobilized probe attached to a solid support. The capture probe was a 58-base oligonucleotide containing a 5' 15-base sequence complementary to a *M. tuberculosis* rRNA sequence, an internal T_{sub.3}, and a 3'dA_{sub.40} tail. The immobilized probe was a poly-dT_{sub.14} sequence attached using carbodiimide chemistry (substantially as previously described by Lund, et al., Nuc. Acids Res.16:10861-10880, 1988) to a solid support of magnetic particles (0.7-1.05 μ l., particles, Seradyn, Indianapolis, Ind.). In this assay, 5 pmol of the capture probe and 50 μ g of immobilized probe particles were used per reaction. The mixture was incubated successively at two different temperatures (60.degree. C. for 20 min, and 25.degree. C. for 15 min). At the first temperature, the *M. tuberculosis*-complementary sequence of the capture probe hybridized to the target sequence because the T_{sub.m} of that hybridization complex is greater than 60.degree. C., and at the second temperature the homopolymeric immobilized probe hybridized to the complementary homopolymeric region of the capture probe because the T_{sub.m} of the dA:dT complex is less than about 50.degree. C. Following both incubations, the magnetic beads were separated from the solution using a magnetic field substantially as described in Example 2. If *M. tuberculosis* was present in the sample, these magnetic beads have attached a hybridization complex consisting of immobilized probe:capture probe:target polynucleotide. If *M. tuberculosis* was not present in the sample, the beads have attached a hybridization complex consisting of immobilized probe and capture probe. The beads were washed twice with 1 ml of washing buffer per wash by resuspending the beads in buffer and then repeating the magnetic separation step. Washed beads were then resuspended in 75 μ l of a nucleic acid amplification reagent solution for transcription associated amplification using methods substantially as described in Kacian et al., U.S. Pat. Nos. 5,399,491 and 5,554,516. The beads and 15 pmol of each primer specific for the *M. tuberculosis* target polynucleotide were incubated in a reaction mixture (40 mM Trizma base, pH 7.5, 17.5 mM KCl, 20 mM MgCl₂, 5% polyvinylpyrrolidone (PVP), 1 mM each dNTP, 4 mM each rNTP), covered with a layer (200 μ l) of inert oil to prevent evaporation, at 60.degree. C. for 10-15 min, and then at 41.5-42.degree. C. for 5 min. Reverse transcriptase (about 750 Units and about 2,000 Units of T7 RNA polymerase in 25 μ l) was added per reaction, mixed, and the amplification of the target polynucleotide proceeded at 41.5-42.degree. C. for 2 hr. Amplified *M. tuberculosis* target sequences were detected using an AE-labeled probe which was detected as chemiluminescence and expressed in relative light units (RLU) substantially as described previously (U.S. Pat. No. 5,658,737 at column 25, lines 27-46; Nelson et al., 1996, Biochem. 35:8429-8438 at 8432). For each assay, a negative control consisting of all of the same reagents but substituting an equal volume of negative sputum for sample, and a positive control consisting of all of the same reagents but including 50 μ l of extracted total cellular *M. tuberculosis* RNA (containing about 2000 copies of rRNA) instead of sample. Duplicate tests were performed (RLU No.1 and No.2 in Table 3).

WEST

L2: Entry 12 of 37

File: USPT

Feb 8, 2000

DOCUMENT-IDENTIFIER: US 6022714 A

TITLE: Methods for attachment of a polynucleotide to a preselected material

BSPR:

Chu et al. have described a potentially simple method for attaching amines to the terminal 5'-phosphate of synthetic polynucleotides (Chu, B. C., Wahl, G. M. and Orgel, L. E., *Nucleic Acids Res.* (1983) 11, 6513-6529.). The authors describe the coupling of uridine monophosphate to simple amines, polylysine and bovine serum albumin and the reaction of ethylene diamine with oligo(dT). The couplings are achieved by treating the 5'-phosphorylated species, either UMP or oligo(dT) with a water-soluble carbodiimide in imidazole buffer to form the corresponding 5'-phosphorimidazolide. The latter activated derivative is then isolated and treated with a large excess of amine to obtain a 5'-phosphoramidate. This chemistry requires a high concentration of amine to compete with water hydrolysis of the intermediate phosphorimidazolide. Because it is difficult to obtain relatively high concentrations of reactive amine groups on proteins and solid supports in an aqueous environment, very low levels of attachment, if any, will be achieved. If an immobilization takes place, a phosphoramidate bond is formed which is reported by Chu et al. to be unstable below pH 7.

WEST

L2: Entry 16 of 37

File: USPT

Jul 13, 1999

DOCUMENT-IDENTIFIER: US 5922535 A

TITLE: Identifying sequence differences in nucleic acid populations

DEPR:

The above discussion also describes an isolation process that involves securing duplexes to a solid phase so that soluble cleavage products can readily be separated therefrom. The embodiment depicted in FIG. 1 and discussed above utilizes a biotin-streptavidin interaction to immobilize duplexes on a solid phase. Other immobilization techniques are well known in the art and can readily be utilized in the practice of the present invention. For example, nucleic acids can be immobilized on poly(ethyleneimine)-modified nylon beads using cyanuric acid as the coupling reagent (see, for example, Ness et al. Nuc. Acids Res. 19:3344, 1991, incorporated herein by reference). Alternatively, carbodiimide-mediated end-attachment either of 5'-phosphate to amino magnetic beads or of 5'-NH₂ -modified nucleic acids to carboxyl magnetic beads can be utilized (see, for example, Lund et al., Nuc. Acids Res. 16:10861, 1988, incorporated herein by reference).

WEST

L2: Entry 17 of 37

File: USPT

Jun 15, 1999

DOCUMENT-IDENTIFIER: US 5912344 A

TITLE: Chemiluminescent group-containing carbodiimide compound

BSPR:

The chemiluminescent group-containing carbodiimide compound of the present invention can be used as the label in the nucleic acid detection method by hybridization using a labelled nucleic acid. Namely, the nucleic acid labelled with the chemiluminescent group-containing carbodiimide compound can be used as a probe for hybridization. The nucleic acid to be assayed can be detected by allowing the nucleic acid to hybridize with the probe to form a nucleic acid-nucleic acid hybrid, removing free probe from the system, and detecting the label contained in the hybrid. In the present invention, the chemiluminescent group-containing carbodiimide compound used as the label can be detected by measuring chemiluminescence intensity and the like, using a chemiluminescence measuring apparatus, a photocounter, and so on. The nucleic acid to be assayed is usually immobilized on a membrane such as nylon membrane and nitrocellulose, prior to measure.

WEST



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L2: Entry 18 of 37

File: USPT

Jun 1, 1999

DOCUMENT-IDENTIFIER: US 5908746 A
TITLE: Method for analyzing biologically active substances

ABPL:

A method is provided, comprising the steps of reacting a biologically active first substance immobilized on a carrier with a second substance capable of specifically binding the first substance, and detecting a non-bound part of the second substance or a bound part of the second substance indirectly bound to the carrier through binding between the first and second substances so that the first substance or the second substance in a sample is analyzed, wherein the carrier carries a compound having 2 to 100 carbodiimide groups, and the first substance is immobilized on the carrier through the carbodiimide groups so that the active substance such as protein and nucleic acid is bound to the carrier conveniently, efficiently, and tightly.

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L2: Entry 25 of 37

File: USPT

Sep 2, 1997

DOCUMENT-IDENTIFIER: US 5663318 A

TITLE: Assay preparation containing capture and detection polynucleotides covalently bound to substrates with a heterobifunctional crosslinking agent

BSPR:

It is an essential feature of nucleic acid absorption to substrates that the strands must be denatured to efficiently immobilize. Accordingly, mobilization often interferes with the ability of a nucleic acid sequence to hybridize in an assay. DNA is commonly immobilized by absorption to nitrocellulose, nylon, or hydroxyapatite. In order for the DNA to remain insolubilized throughout the assay the strand must be of sufficient length to form several attachment points, this form of absorption often slows the ability of immobilized target DNA to efficiently reanneal with labeled probe DNA. Low molecular weight oligonucleotides and RNA are usually immobilized through a process of absorption and covalent attachment to nylon membranes. For covalent attachment to occur amines on the target sequence must be crosslinked to amines on the support. For single strand DNA, RNA and oligonucleotides the free amines of adenine, guanine, and cytosine are often utilized, rendering these bases unavailable for use in forming interstrand diagnostic interactions with labeled probe. Several previous attempts have utilized artificial nucleotides that have free amine groups available for crosslinking. These molecules must be added to the probe strand prior to linking to the amine on the support. One example employs synthetic nucleotide triphosphates with aminoalkyl function groups extending from the base, added to the 5' end of a DNA chain using polynucleotide kinase. This form of an attachment has some use for double strand DNA where amine bearing residues are blocked by interstrand hydrogen bonds, but offers little advantage for single strand DNA and RNA. Covalent crosslinking of polynucleotides to nylon membranes is also accomplished by generation of photoadducts. This process involves the separate steps of absorbing DNA or RNA to a nylon membrane, drying the membrane and using ultraviolet light (usually 254 nm wavelength) to nonspecifically attach bases to the free amines of the nylon. Covalent attachment of nucleotides often renders the DNA useless for diagnostic purposes. For example, crosslinking of amines and carboxylic acids using carbodiimide methods that work well for proteins will render nucleic acids insoluble through interstrand covalent bonds. Aldehydes, such as glutaraldehyde, can attach to hydroxyl groups throughout the length of the polymer's sugar backbone rather than at specific loci, and may crosslink strands together preventing annealing with a labeled probe sequence.

WEST

L2: Entry 27 of 37

File: USPT

Mar 11, 1997

DOCUMENT-IDENTIFIER: US 5610287 A
TITLE: Method for immobilizing nucleic acid molecules

ABPL:

Synthetic nucleic acid molecules are non-covalently immobilized in the presence of a salt or cationic detergent on a hydrophilic polystyrene solid support containing an --OH, --C.dbd.O or --COOH hydrophilic group or on a glass solid support. The support is contacted with a solution having a pH of about 6 to about 8 containing the synthetic nucleic acid and the cationic detergent or salt. Preferably, the cationic detergent is 1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride at a concentration of about 30 mM to about 100 mM or octyldimethylamine hydrochloride at a concentration of about 50 mM to about 150 mM. The salt is preferably NaCl at a concentration of about 50 mM to about 250 mM. When the detergent is 1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride, the glass support or the hydrophilic polystyrene support is used. When NaCl or octyldimethylamine hydrochloride is used, the support is the hydrophilic polystyrene. After immobilization, the support containing the immobilized nucleic acid may be washed with an aqueous solution containing a non-ionic detergent. The immobilized nucleic acid may be used in nucleic acid hybridization assays, nucleic acid sequencing and in analysis of genomic polymorphisms.

CLPV:

(a) contacting said support with a solution having a pH of from about 6 to about 8, and containing said nucleic acid and (1) a cationic detergent selected from the group consisting of 1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride provided at a concentration of from about 30 mM to about 100 mM, and octyldimethylamine hydrochloride provided at a concentration of from about 50 mM to about 150 mM or (2) NaCl provided at a concentration of from about 50 mM to about 250 mM, to thereby non-covalently immobilize said nucleic acid to said support, wherein:

PUB-NO: US005610287A

DOCUMENT-IDENTIFIER: US 5610287 A

TITLE: Method for immobilizing nucleic acid molecules

PUBN-DATE: March 11, 1997

INVENTOR-INFORMATION:

NAME	COUNTRY
NIKIFOROV, THEO	US
KNAPP, MICHAEL R	US

INT-CL (IPC): C07H 21/04; C12Q 1/68; C12N 15/00; C12N 11/08

EUR-CL (EPC): C07H001/08; C12Q001/68

ABSTRACT:

Synthetic nucleic acid molecules are non-covalently immobilized in the presence of a salt or cationic detergent on a hydrophilic polystyrene solid support containing an -OH, -C=O or -COOH hydrophilic group or on a glass solid support. The support is contacted with a solution having a pH of about 6 to about 8 containing the synthetic nucleic acid and the cationic detergent or salt. Preferably, the cationic detergent is 1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride at a concentration of about 30 mM to about 100 mM or octyldimethylamine hydrochloride at a concentration of about 50 mM to about 150 mM. The salt is preferably NaCl at a concentration of about 50 mM to about 250 mM. When the detergent is 1-ethyl-3-(3'-dimethylaminopropyl)-1,3-carbodiimide hydrochloride, the glass support or the hydrophilic polystyrene support is used. When NaCl or octyldimethylamine hydrochloride is used, the support is the hydrophilic polystyrene. After immobilization, the support containing the immobilized nucleic acid may be washed with an aqueous solution containing a non-ionic detergent. The immobilized nucleic acid may be used in nucleic acid hybridization assays, nucleic acid sequencing and in analysis of genomic polymorphisms.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KMC](#) | [Drawn Desc](#) | [Image](#)

35. Document ID: EP 747703 A2

L2: Entry 35 of 37

File: EPAB

Dec 11, 1996

WEST

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Search Results - Record(s) 41 through 50 of 50 returned.

41. Document ID: US 4731325 A

L5: Entry 41 of 50

File: USPT

Mar 15, 1988

US-PAT-NO: 4731325

DOCUMENT-IDENTIFIER: US 4731325 A

TITLE: Arrays of alternating nucleic acid fragments for hybridization arrays

DATE-ISSUED: March 15, 1988

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Palva; Airi M.	Helsinki	N/A	N/A	FIX
Ranki; Tuula M.	Espoo	N/A	N/A	FIX
Soderlund; Hans E.	Espoo	N/A	N/A	FIX

US-CL-CURRENT: 435/6; 435/5, 435/91.41, 435/91.52, 436/501, 536/24.3, 536/24.32

ABSTRACT:

The invention is related to improved nucleic acid reagents comprising arrays of nucleic acid fragments and combinations of such fragments. The preparation of such fragments by recombinant DNA techniques and their use in sandwich hybridization methods is also described. By making different combinations of the nucleic acid fragments--some labeled and some affixed to solid carriers, it is possible to create kits for the identification of e.g. venereal diseases.

The improved nucleic acid reagents comprise two series of at least two alternating nucleic acid fragments, which are homologous to sequences in the nucleic acid to be identified, one of the series being labeled and one affixed to a solid carrier. Nucleic acid fragments belonging to different series must not be homologous to each other.

Sandwich hybridization tests performed with arrays of nucleic acid fragments are at least four times as sensitive as sandwich hybridization tests performed with reagents belonging to the prior art.

22 Claims, 13 Drawing figures Exemplary Claim Number: 21
Number of Drawing Sheets: 8

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#) [Claims](#) [IOMC](#) [Draw. Desc](#) [Image](#)

42. Document ID: US 4811218 A

L5: Entry 42 of 50

File: EPAB

Mar 7, 1989

DERWENT-ACC-NO: 2001-161549
 DERWENT-WEEK: 200128
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TITLE: Nucleic acid detection method for detecting presence of gene mutation for diagnosing cancer and viral infections, involves using complementary arrays and labeled nucleic acid probes

PRIORITY-DATA: 1999JP-0283148 (October 4, 1999), 2000JP-0191477 (October 4, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2001103999 A	April 17, 2001	N/A	008	C12Q001/68
JP 3103806 B1	October 30, 2000	N/A	006	C12N015/09
JP 2001095570 A	April 10, 2001	N/A	006	C12N015/09

INT-CL (IPC): C12M 1/00; C12M 1/40; C12N 15/09; C12Q 1/25; C12Q 1/68; G01N 33/50; G01N 33/53; G01N 33/536; G01N 33/566

ABSTRACTED-PUB-NO: JP 3103806B

BASIC-ABSTRACT:

NOVELTY - Flag arrays FL1-FLn are formed using labeled probes B1-Bn connected to second partial sequence of S1'-Sn' include complementary to second partial array S1-Sn of target nucleic acid, which is then hybridized to labeled first probes A1-An connected to complementary F1'-Fn' array of first partial array F1-Fn of target nucleic acid.

DETAILED DESCRIPTION - Complementary arrays FL1'-FLn' is formed by hybridizing, probes A1-An and B1-Bn. This complementary array is hybridized to FL1-FLn and the bound probes are released. The probes are measured and target nucleic acid is measured.

Detecting a target nucleic acid having a predetermined sequence N1-Nn (n = 2 or more integers) in a biological sample involves using complementary array F1'-Fn' for partial array F1-Fn of target nucleic acid. F1'-Fn' comprises a first probe A1-An comprising a labeled substance. A second complementary array S1'-Sn' connected to second probe B1-Bn attached with flag arrays FL1-FLn is also provided against second partial array S1-Sn of target nucleic acid. The probes and sample are mixed to form hybridization between F1-Fn and A1-An, and S1-Sn with B1-Bn. In the next step, probes A1-An and B1-Bn are blended to form (A1+B1)-(An+Bn) to form complementary array FL1'-FLn' which is then hybridized to flag arrays FL1-FLn. The probes (A1+B1)-(An+Bn) released after hybridization are collected and the label is measured. Target nucleic acid in the sample is detected.

USE - For detecting mutations in the nucleic acid in biological samples for diagnosing cancer, viral infections, etc.

ADVANTAGE - The method is specific, simple and versatile.

DESCRIPTION OF DRAWING(S) - The figure shows the nucleic acid detection method using labeled probes and complementary nucleic acid arrays.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Draw Desc	Clip Img	Image
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□ 45. Document ID: AU 200052696 A, WO 200070093 A1

L5: Entry 45 of 50

File: DWPI

Dec 5, 2000

DERWENT-ACC-NO: 2001-016252
 DERWENT-WEEK: 200113
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